REMARKS

Claims 63-82 and 84 are pending in this application.

By the present amendment, claims 70 and 77 have been amended to further clarify the present invention. Claims 79 to 82 have been canceled. Applicants reserve their rights to file a continuation application on the canceled subject matter. New claims 85 to 92 have been added. Support for these claims is found, for example, in the original claims and with respect to the claim elements human thioredoxin or glutaredoxin can be found at least in paragraph [0044] in the application as filed. No new matter has been added by these amendments.

Claim rejections under 35 U.S.C. § 112, first paragraph

Claims 63-65 and 77-82 and 84 have been rejected under 35 U.S.C. §112, first paragraph as lacking enablement. As far as this rejection may pertain to the amended claims, this rejection is respectfully traversed.

In rendering this rejection, the Office deems that it would require undue experimentation for the person skilled in the art to practice the invention since the claims read broadly on intracellular recognition molecule fragments or any target or platform. Applicants respectfully disagree with the Office's conclusion for the following reasons.

The presently claimed invention stems in large measure from the finding that, for any given target molecule, a recognition partner with an interaction K_d value of less than or equal to $5x10^{-9}$ M can be designed, with the recognition partner having the specific structure of a peptide aptamer according to claim 63. This recognition molecule may also be found by screening a library of aptamers having the specific structure required by claim 63.

Since the sequence of a peptide aptamer according to claim 63 is dependent on the target molecule, to recite all aptamers covered by claim 63 would require lists of information, none of which is needed to practice the present invention without undue

experimentation. Rather, the present specification provides sufficient information for the skilled person to design or identify a peptide aptamer interacting with a chosen target molecule with a K_d value of less than or equal to $5x10^{-9}$ M.

Specifically, the present application, including the experimental section, provides examples of such peptide aptamers. This experimental section also provides sufficient details for preparing a library of peptide aptamers having the thioredoxin protein as a platform and a variable region, inserted into the platform, which is 20 amino acids in length. Moreover, the claims have been amended to make clear that the peptide aptamers necessarily interact with a target molecule with a K_d value of less than or equal to $5x10^{-9}$ M. This feature is an important aspect of the peptide aptamers of the presently claimed invention. The application teaches how to screen for aptamers, in such a library, which interact with a given target with a K_d value of less than or equal to $5x10^{-9}$ M (see, for example, page 7, [0023], page 26, [0109], and the Examples).

The Office deems that "[i]t is no way predictable that random mutations such as deletions, substitutions etc. would result in a protein having activity compared to the one disclosed." However, Applicants submit that the specification, including the Examples, clearly illustrates to the person skilled in the art how to obtain higher-affinity recognition partners having the claimed characteristics of the peptide aptamers of the present invention using random mutagenesis. The Office has provided no reasoning why such an approach would not work, nor evidence countering Applicants' assertion that high-affinity recognition partners could readily be obtained by such a technique.

The Office relies on Wells to support the general notion of unpredictability. However, Wells relates to enzyme function and not to aptamer binding. Therefore, this reference is not applicable to the presently claimed invention, which is a different technology.

Furthermore, the Office appears to conclude that "it is not routine to screen large numbers of mutated proteins where the expectation of obtaining similar activity is

unpredictable." Once again, Applicants submit that it is routine for the person skilled in this particular art to screen mutated proteins following the examples set forth in the specification. Indeed, the specification clearly describes how to measure a gain in binding affinity, for example, by using a LexAop-GFP reporter gene to quantify the binding reactions, followed by plotting the fluorescence against K_ds measured in evanescent wave experiments. These described methods are routinely used in the art and provide predictable methods for determining increases in affinity.

Thus, in view of the above, it is submitted that, contrary to the Office's assertion, the skilled artisan would not recognize a high degree of unpredictability because the application teaches methods for the identification of a recognition peptide aptamer for a given target molecule. The only experimentation needed is to design a peptide aptamer library and to screen the library according to the teachings of the specification. Applicants submit that this would not be considered undue experimentation, but merely routine for the person skilled in the art.

Moreover, the Office deems that "thioredoxin-like proteins," as indicated in the claims, are not enabled since none are disclosed in the specification. Applicants submit that this term is well known in this art, as evidenced by the enclosures in Annex I, all of which use this term of art. As stated by the Federal Circuit in *S3 Inc. v. nVIDIA Corp.*, 259 F.3d 1364, 1371, 59 USPQ2d 1745 (Fed. Cir. 2001):

> The law is clear that patent documents need not include subject matter that is known in the field of the invention and is in the prior art, for patents are written for persons experienced in the field of the invention.

Applicants submit that those skilled in the art would know what "thioredoxin-like proteins" are, and could make and use them accordingly.

Finally, in support of the enabling nature of the present specification, Applicants enclose a second Declaration of Dr. Pierre Colas. This Declaration provides experimental results of peptide aptamers against adaptor protein Grb2 and the protein kinases Raf and

ERK1 to substantiate the claims made in the last Declaration, as requested by the Office.

In view of the above, Applicants submit that the presently claimed invention is enabled and withdrawal of this rejection is respectfully requested.

Claim rejections under 35 U.S.C. § 112, second paragraph

Claims 77-82 stand further rejected under 35 U.S.C. §112, second paragraph as being indefinite. This rejection should be rendered moot in view of the present amendments.

More specifically, claim 77 has been amended to recite "each being an intracellular recognition molecule according to claim 63," as suggested by the Office. Claims 79 to 82 have been deleted. Withdrawal of this rejection is respectfully requested.

Claim Rejections under 35 U.S.C. § 102

Claim 79 has been rejected under 35 U.S.C. § 102(b) as being anticipated by Brent et al, WO96/02561 and Colas et al., Nature, vol. 380 (1996). In addition, claims 79-82 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Colas et al, TIBTECH vol. 16 (1998).

By the present amendment, claims 79-82 have been deleted solely to expedite the prosecution of the present application and not to acquiesce to the Office's rejections, which should render these rejections now moot. Withdrawal of the § 102 rejections is respectfully requested.

Attorney Address Correction

Applicants note that the Office action was mailed to the incorrect address. Effective immediately, please address all communication in this application to:

Karen L. Elbing, Ph.D.
Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
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Conclusion

Applicants submit that this application is now in condition for allowance, and such action is respectfully requested. Enclosed is a Petition to extend the period for replying to the Office action for three months, to and including February 27, 2006, since February 25th falls on a Saturday, and a check in payment of the required extension fee.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 27 Febrny 2006

Karen L. Elbing, Ph.D.
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